REMARKS

Claims 85-92 and 107-113, 115-118 are pending. Claims 85, 90, 107, 109-112, 115, and 118 have been amended to clarify that the output is at least to a user. Applicants note that the claims still allow for an output to a memory in addition to the output to the user. Support for the amendments can be found in the specification and original claims, for example Claims 11, 12, 41, and 79 and paragraphs **0032**, **0111**, **0139**, and **0152-0154** (of the online USPTO publication) and the abstract. No new matter has been added by these amendments. Claim 114 has been cancelled. This is not a surrender of subject matter and Applicants reserve the right to pursue the cancelled subject matter at a later point in time.

Applicants thank the Examiner for acknowledging the withdrawal of the rejections of Claims 85-92, 107-109, 111, and 118 under 35 U.S.C. §112 and Claims 85-92, 109-118 under 35 U.S.C. §103(a).

Amended Claims 85-92, 107-109, 111, and 118 are Directed to Statutory Subject Matter.

The Examiner has asserted that outputting data to a memory "is not a tangible result because it does not communicate a result to a user in a user readable format." (O.A. p. 3). While the Examiner has cited no support for this legal requirement, the Examiner has noted that the rejection would be overcome by amending the claims to outputting data "to a user."

While the Applicants do not necessarily agree with the Examiner's rejection, Applicants have amended the relevant independent claims as requested by the Examiner. As such, Applicants submit that the claims are directed to statutory subject matter. Applicants request that the Examiner withdraw the rejection and allow the claims. Applicants also note that the claims are also clearly linked in their application to a computer and are further statutory subject matter for at least this reason as well.

Claims 85-92 and 109-118 are nonobvious over Daniel et al. in view of Wang et al.

The Examiner has asserted that Claims 85-92 and 109-118 are obvious in light of Daniel et al. (*J. of Immun.*, 162: 617-624, 1998) in light of Wang et al. (J. of Mol. Modeling, 4:379-394, 1998). The Examiner has asserted that Daniel teaches two different methods for predicting binding affinities between MHC class I proteins and epitopes. In addition, the Examiner has

asserted that "it would have been obvious to combine first and second scaled binding affinities, since Daniel shows comparing the same experimental data from two different predictive methods and adjusting the data such that all data is compared on the same scaling range...." (O.A. p. 6). The Examiner has asserted that the motivation for doing this "would have been to obtain a consensus binding affinity from different predictive methods." (Office Action, p. 6). Applicants respectfully traverse the rejection and submit that Daniel does not actually teach the element noted above by the Examiner. In addition, not only does Daniel fail to teach any reason for combining the two different methods, but Daniel clearly further establishes that one of skill in the art would not have combined results that were generated by two different methods, as recited in the present claims. These issues are discussed in detail below.

Daniel Does Not Teach Two Methods of Predicting Binding Affinities between **MHC and Epitopes.**

As an initial point, Applicants note that Daniel is not studying the interaction and affinities of MHC and peptides, but rather of peptides and the "TAP transporter." (See abstract and paper generally). For example, Daniel's abstract clearly states that the neural network predictions were used to obtain TAP affinities. The Examiner's confusion may have stemmed from the phrase "HLA class I ligands" (p. 618) and similar such terms. However, when read in context, it is clear that these "HLA ligands" are not actually HLA proteins, but ligands that bind with HLA proteins as well as to TAP transporters.

As such, Daniel's calculations are actually directed to the interaction of ligands to TAP proteins, and are not predicting affinities of HLA molecules. Thus, Daniel does not actually teach predicting binding affinities between MHC proteins and epitopes. As such, not all of the elements have been taught and a *prima facie* showing of obviousness has not been established. Applicants request that the rejection be withdrawn and the claims allowed.

Daniel **Teaches Away** from Combining the First and Second Affinities

As acknowledged by the Examiner, Daniel does not teach combining the first and second binding affinities as in Claims 85, 90, 107-112, and 118 (O.A. p. 6). Instead, the Examiner has asserted that one of skill in the art would have been motivated to combine the first and second

scaled binding affinities because "Daniel shows comparing the same experimental data from two different predictive methods and adjusting the data such that all data is compared on the same scaling range." (O.A. p. 6). The Examiner has further asserted that the motivation to do this would have been to "obtain a consensus binding affinity from different predictive methods." (O.A. p. 6). Applicants respectfully disagree with the Examiner's interpretation of Daniel.

As discussed in the previous responses, one of skill in the art would not have combined two different methods as recited in the claims. Indeed, Daniel itself serves as further proof that one of skill in the art would not have combined the various affinities in the manner claimed. Simply put, Daniel teaches away from combining the two different predicted affinities.

As noted in the previous Responses, the combination of two different predictions was counterintuitive and generally taught away from, as those in the art believed that one method would work better than the other. In particular, the various publications cited by the Examiner (including Daniel) contrasted the various methods of prediction so that they could select one method over the others. The unmistakable implication being that one method would be more accurate than the other methods. To put it another way, those of skill in the art were laboring under the impression that one model would be accurate while the other models would be inaccurate (or less accurate). As a result of this, in each of the previously cited references, as well as in Daniel, the author selected only one of the methods as the "superior" method and used that method for their remaining experiments. Indeed, this reasoning is explicitly put forth in Daniel when he states that:

> the superior performance of ANNs suggests that consideration of these effects by predictive tools is possible and necessary for universally applicable prediction of TAP affinity. For further analyses, we therefore used ANN-based predictions."

(p. 620, col. 2, emphasis added). Thus, it is clear that Daniel was not "comparing" these various methods to combine them (as suggested by the Examiner), but contrasting these various methods in order to drop the less accurate methods.

Thus, even this most recently cited reference does not support the Examiner's assertion that "it would have been obvious to combine first and second scaled affinities," or that "the motivation would have been to obtain a consensus binding affinity from different predictive methods." (O.A. p. 6). Indeed, going by the actual disclosure in Daniel, Daniel clearly teaches

away from combining two different predictive methods. Given that Daniel does not teach the Examiner's proposed motivation, and actually teaches away from the claimed combination, Applicants respectfully request that the rejection be withdrawn and the claims be allowed.

Applicants note that Wang neither addresses Daniel's failings noted above, nor has it been asserted as teaching aspects that remedy these failings. Moreover, Applicants respectfully disagree with the Examiner's characterization of Wang. The Examiner has asserted that the 6 "scores" taught in Wang represent 6 different binding affinities (O.A. p. 7). However, it is clear from the cited section in Wang that the values being combined are each part of a single change in free energy. In particular, Wang explicitly states that "[w]e assume that the free energy change in the protein-ligand binding process can be dissected into basic components." (Emphasis added, p. 384, col. 1). Thus, Wang is actually talking about multiple components in a single free energy prediction, not combining individual affinity predictions. As such, the cited section of Wang is simply not relevant to the instantly claimed invention and does not teach the elements that the Examiner asserts it to teach.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and request the same. If, however, some issue

remains that the Examiner feels can be addressed by Examiner Amendment, the Examiner is cordially invited to call the undersigned for authorization.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 01-2213.

Respectfully submitted,

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